Michigan Department of Community Health

MDCH

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LabLink

Laboratory Information from the Michigan Department of Community Health - Bureau of Laboratories

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Hepatitis A Update

Frances Pouch Downes, Dr. P.H.
Acting Laboratory Director

Hepatitis A case reports from southeast Michigan have increased dramatically over the past two years. Laboratory leaders in that area have been contacted to assist in the public health efforts. The epidemiological data resulting from initial investigations indicate that this increase is not an easily defined outbreak: no food or water vehicle has been identified, behavioral risk factors appear to be complex and a number of the cases are quite sever. The public health response and control of this epidemic have been stymied by several laboratory issues identified below. Suggested action steps for the clinical laboratory community are presented in this letter.

Issue 1: Routine use of hepatitis panels which includes total anti-HAV antibody only.

Many laboratories offer a hepatitis panel (80059 CPT code) which includes "Hepatitis A (HAAb), IgG and IgM." Clinicians tend to order this panel because it is available on the test request form and they may be unaware that IgM testing is not included in the standard hepatitis panel.

Issue 2: Reporting total HAV antibody to local public health, or not reporting at all.

The Michigan Communicable Disease Rules require that laboratory directors report the results of thirty-eight (38) infectious disease tests to the local health department in the county of the patient's residence. Hepatitis A (IgM) is one of these reportable results.

In Michigan, as in other parts of the U.S., most ill persons seek medical care from their health care provider, not a public health agency. Each clinical laboratory plays an essential first-line role in recognition of cases which in aggregate identify a community health problem, in this case hepatitis A. Each individual reported case is included in an aggregate analysis of disease activity. Local public health epidemiologists use laboratory reporting data to rapidly identify contacts and offer appropriate prevention education and immune prophylaxis. Aggregate data derived from case reports are used to describe populations at risk for infection and to target prevention efforts.

Action Step 1: Offer clinically useful tests.

The CPT Board of the American Medical Association has revised the standard hepatitis panel to include hepatitis A IgM. This change will not be implemented until the publication date of the next manual (January 1, 2000). On April 30, 1999, the Centers for Disease Control and Prevention (CDC) recommended that prior to January 1, 2000, clinical laboratories offer individual tests for IgM (CPT 86709) for accurate determination of the cause of illness in patients with signs/symptoms of acute viral hepatitis (MMWR, 1999, 48(16)).

(Continued on page 2)

(Continued from page 1)

Several laboratories in Michigan have already taken steps to assure that clinically relevant test panels are available and that billing for these services is accurate. Quest Laboratories of Auburn Hills has put together an Acute Hepatitis Panel which consists of hepatitis B surface antigen (CPT 87340), hepatitis B core IgM (CPT 86705), HAV IgM (CPT 86709) and hepatitis C antibody (CPT 86803). A similar approach by Hospital Consolidated Laboratories in Southfield has been successful, especially with in-patient diagnosis.

Action Step 2: Report positive IgM results promptly to the local health department.

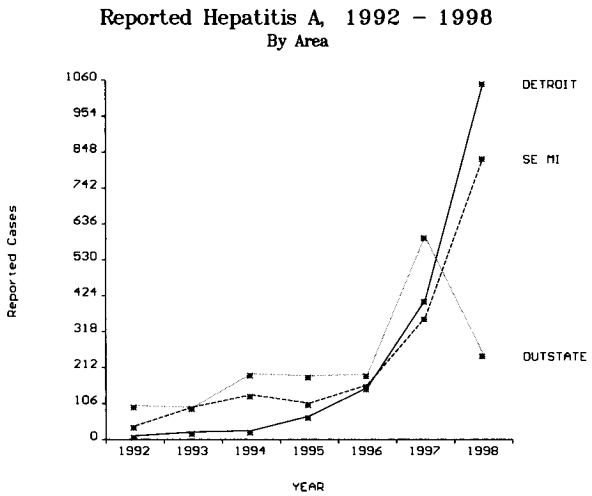
Reporting total HAV antibody results slows down public health by diverting investigations to decades-old infections.

To prevent infection in an exposed individual, immune prophylaxis must be given as soon as possible, but within two (2) weeks of exposure to the virus. Public health staff must locate and recommend or administer this essential prevention. Prompt laboratory reporting is essential in disease prevention and interruption of virus transmission.

Action Step 3: Refer serum specimens to MDCH laboratory.

The Michigan Department of Community Health (MDCH) laboratory is available as a resource for referral of positive total HAV results for IgM testing. The laboratory is also developing a HAV genotyping assay which will contribute molecular epidemiological data needed to investigate clusters and outbreaks of HAV infections.

The role of the community clinical laboratory in delivering clinically relevant data is implicit. The clinical laboratory has an additional essential role to play in population-based control of infectious diseases. By adopting appropriate test menus and promptly reporting positive IgM results to the local public health department, the clinical laboratory plays an essential role in disease control. Questions regarding hepatitis A reporting should be directed to the local health department.



NOTICE:
Change in Viral Serology Methods

The viral serology/viral isolation unit will no longer be performing immune adherence (IA) testing. This assay is a modified complement fixation test that historically has been used to detect viral antibodies in sera and cerebral spinal fluid (CSF). Over the last several years ELISA technology has replaced the IA for serum antibodies. For the last year the only samples tested by IA have been CSF for central nervous system viruses. It is now recognized that this method of diagnosis has little medical value and this testing can be performed by other methods that yield more meaningful results.

The recommended method for herpes virus (HSV) detection in CSF is PCR. The molecular biology laboratory at MDCH is currently working on the development of this assay. In the interim, we recommend culturing all CSF samples when considering herpes infection. The recommended method for mumps virus detection in CSF is culture. The virology laboratory at MDCH will continue to accept CSF samples for HSV and mumps viral cultures.

Submitters who send a CSF sample to the viral serology laboratory, with a request for CNS virus antibodies (test code 2630), will be phoned and asked if they would like to have the sample cultured for HSV and mumps virus. When ordering these assays, order test code 2210 for HSV isolation and 2250 for mumps isolation.

The discontinuation of the Immune Adherence assay will not impact arbovirus testing on CSF in the summer months. The arbovirus assay will still be available for sera or CSF samples. To order arbovirus testing use test code 2770 when submitting a specimen.

INFLUENZA SEASON ENDING

Patty Clark, M.P.H.
Viral Serology/Viral Isolation Unit

During the 98/99 respiratory season virus isolation at the MDCH laboratory included 3 Respiratory synctial virus (RSV), 7 Parainfluenza virus, 32 influenza type A (H3N2), and 19 influenza type B (B/Beijing/184/93-like) virus. As reported in *LabLink* Vol 4, No.3 (Winter 1999), influenza A (H3N2) was the predominant strain recovered by culture at MDCH from October 1998 through January 1999. Influenza A (H3N2) was also the predominant strain recovered from January 1999 through April 1999.

The MDCH laboratory isolated sporadic cases of influenza from early November 1998 through mid-January 1999. By the end of January isolates were predominantly influenza B (B/Beijing/184/93-like). By early February the laboratory was recovering influenza A (H3N2) on a daily basis with only an occasional influenza B (B/Beijing/184/93-like). Isolates were submitted from all over the state with no localized pockets observed.

This year's vaccine contained antigens for influenza A (H1N1) [A/Beijing/262/95-like]; influenza A (H3N2) [A/Sydney/05/97-like]; and influenza B [B/Beijing/184/93-like]. The strains recovered at the MDCH laboratory this season were a good match with this year's vaccine.

Interesting Websites

1. *The President's Council on Food Safety may be found at:*
   www.foodsafety.gov/ presidentscouncil

2. *Parasitology images and diagnosis can be found at:*
   www.dpd.cdc.gov/dpdx

HIV-1 Viral Load Update

Deborah Stephens, MT (ASCP)
HIV Unit

The HIV-1 viral load test is used in conjunction with clinical presentation and other laboratory markers of disease progress for the clinical management of HIV-1 infected patients. The test can be used to assess patient prognosis by measuring the baseline HIV-1 RNA level or to monitor the effects of antiretroviral therapy by measuring changes in plasma HIV-1 RNA levels during the course of antiretroviral treatment. With the recent use of highly active antiretroviral therapy (HAART), a significant number of clients attain viral loads below the detectable limit. MDCH offers Roche's "standard" HIV-1 Monitor Test of the lower detectable range of 400 copies/mL. Studies show lower viral loads are associated with better outcomes and demonstrate a longer time to treatment failure than those with detectable viral loads above the detectable limit.

FDA has recently approved the Roche Amplicor Ultra Sensitive HIV-1 Monitor Test. The new ultra sensitive RT-PCR method allows detection and quantitation of HIV-1 RNA levels below the sensitivity limits of other viral load assays. The linear dynamic range of this new method is from 50-75,000 copies/mL of plasma and overlaps the range of the standard method. Therefore, when the viral load of clients falls below 75,000, subsequent monitoring may be done using the ultra sensitive method.

Currently, Roche anticipates that the ultra sensitive assay will be available sometime in June of this year. When the product is available for purchase, MDCH will begin offering the service. The new ultra sensitive test will be performed as indicated. This service is limited to clients enrolled in the MDCH HIV/AIDS Drug Assistance Program, Medicaid and the Children's Special Health Care Service or by special arrangement. To receive specimen containers and test request forms phone (517) 335-9867.

Questions regarding enrollment in the ADAP program should be directed to Merry Gastambide at (517) 335-9333. For questions regarding technical/laboratory issues contact Deborah Stephens or Bruce Robeson at (517) 335-8098.

Quirky bugs ...

Group A Streptococcal Disease (GAS)

Sandip Shah, MS, MT(ASCP)
Reference Bacteriology

Genesee County Health officials determined that chicken pox, a vaccine preventable disease*, combined with a common group A streptococcal infection likely led to the recent death of an 8-year-old boy in Fenton, Michigan. While group A streptococcal infections are common, death from the disease is rare. This case, along with other clusters within the state and around the country, has alerted the public health community to be more vigilant regarding this disease. Some argue that group A *Streptococcus* spp. is the quintessence of an old organism that has become more virulent and therefore it is an emerging pathogen.

Group A streptococcus (GAS) is a bacterium commonly found in the throat and on the skin. The letter A refers to a serological classification of bacteria in the genus *Streptococcus* according to the composition of the cell wall. GAS can be further classified into m serotypes also based on cell wall components. GAS can be present in the throat or on the skin and cause no symptoms of disease. They may also cause infections that range from mild to severe or life-threatening. GAS is spread by direct contact with secretions from the nose and throat of infected persons or by contact with infected wounds or sores on the skin. The risk of spreading the infection is highest when a person is ill or has an infected wound. Persons who carry the bacteria but have no symptoms are less contagious. Treatment of infected persons with an appropriate antibiotic for 24 hours or longer generally eliminates their ability to spread the bacteria.

The majority of GAS infections are relatively mild illnesses, such as "strep throat," cellulitis or impetigo. Occasionally these bacteria can reach parts of the body where bacteria are not usually found, such as the blood, deep muscle, fat tissue or lungs. This may occur when the patient infected is immunosuppressed or has other underlying conditions like diabetes, alcohol/IV drug abuse, trauma/surgery, postpartum, varicella (chicken pox), open sores or other breaks in the skin that allow the bacteria to get into the tissue causing invasive infection. The most severe but least common forms of invasive GAS disease are necrotizing fasciitis (NF) and streptococcal toxic shock syndrome (STSS). Necrotizing fasciitis (sometimes described by the media as the flesh-eating bacteria) is a severely painful, destructive infection of muscle and fat tissue. Streptococcal toxic shock syndrome is a rapidly progressing infection causing shock, injury and failure to internal organs including the kidneys, liver and lungs. Worldwide, rates of NF and STSS increased from the mid-1980s to the early 1990s. Increases in the rate and severity of disease have been associated with increases in prevalence of M-1 and M-3 serotypes. The CDC began national passive surveillance for invasive infection and STSS in 1995, with active laboratory-based surveillance in the Emerging Infection Program sites.

According to CDC estimates the yearly incidence rate in the U.S. is approximately 10,000 to 15,000 cases of invasive GAS disease (4/100,000 population) resulting in over 2,000 deaths. Approximately 20% of patients with necrotizing fasciitis and 60% of patients with STSS die annually in the U. S. This compares with a mortality rate of 10% to 15% in patients with other forms of invasive GAS disease. In contrast, over 10 million persons get "strep throat" and impetigo annually, with 97% of the treated patients becoming culture negative within 24 hours. Penicillin, cephalosporins and their derivatives remain the drugs of choice. Erythromycin resistant strains have been reported in many countries, most recently in Spain and Italy.

Detection of GAS in the laboratory is one of the least standardized procedures in clinical microbiology. Accurate interpretation is dependent upon the competence of the laboratory personnel, methodology and quality of specimen.

Important culture isolation factors include:

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A. Method of inoculation onto plates - The entire surface of the swab must make contact with the plate and the plate must be streaked for isolation.

B. Composition and quality of media - Only properly quality controlled enriched media, without inhibitors should be used.

C. Atmosphere during incubation - Aerobic with 5% CO_2 or an anaerobic jar.

D. Duration of incubation - 48 hours. 10% or more of GAS could be missed on primary plates at 24 hours.

E. Method of identification - Beta hemolysis coupled with bacitracin resistance is still the best primary identification method. Immunological confirmation is still recommended either by precipitin test, flourescent antibody or latex agglutination.

F. Technical expertise - Culture work and interpretation must be done by a competent and experienced microbiologist.

CDC is investigating an alternative genotyping system for GAS isolates (*emm* typing). This will allow better strain identification as compared to serotyping and other molecular techniques like PFGE. Challenges lie ahead for public health community to improve recognition and diagnosis by clinicians; evaluate adjunctive therapy with intravenous immune globulin for STSS and NF; investigate organism virulence factors; define role of the host immune response in STSS; develop control strategies to prevent spread in families, institutions and other high-risk settings along with educational programs for these groups.

* An effective vaccine against varicella is now available and recommended for use in all children who have not previously had the chicken pox. Immunization of children against varicella could prevent similar GAS infections in the future.

References

1. R. Facklam et al, "*emm* Typing and Validation of Provisional M Types for Group A Streptococci," Emer. Inf. Diseases 5:2, 1999, pp. 247-253.

2. Dennis L. Stevens, "Streptococcal Toxic-Shock Syndrome: Spectrum of Disease, Pathogenesis, and New Concepts in Treatment," Emer. Inf. Diseases 1:3, 1995, pp. 69-78.

New Food and Flu Epidemiologist

Sally A. Bidol, BSN, MPH, has joined the MDCH Bureau of Epidemiology, Communicable Disease Epidemiology Division, as an epidemiologist responsible for surveillance of foodborne illnesses and monitoring of influenza activity and patterns. She will be the first-line contact within the division for consultation and investigation pertaining to foodborne disease clusters and outbreaks. She will also maintain a statewide, sentinel surveillance system for cases of influenza, including detection of emerging variant strains.

Bidol obtained a master's degree in epidemiology from the University of Michigan, School of Public Health, and also has a clinical background in nursing. Bidol previously worked as an epidemiologist for the HIV/AIDS surveillance section in Detroit. She can be reached at the division office in Lansing at (517) 335-8165 or at e-mail address ***<bidols@state.mi.us>***.

New Employees at the Bureau of Laboratories

MDCH and the Bureau of Laboratories (BOL) would like to welcome the following new employees. Anuradha Patel was an employee for the bureau assigned to the Detroit City Health Department. She now works in the microbiology section. Kevin Rodeman comes to the molecular biology section from BioPort. Nirmala Shah also joins BOL from BioPort. She is currently in the virology section but will soon split her work schedule between virology and microbiology.

BOL would also like to announce the transfer of two employees. Debra Groh has left the microbiology section and is now the departmental supervisor in the data acquisition and specimen handling unit. Judith Kloss Smith has left the chromatography unit in microbiology and is now the quality control officer in the office of quality assurance.

CONFIRMATORY TESTING FOR HEPATITIS C VIRUS: SERUM ACCEPTABLE FOR PCR

Jeff Massey, Dr. P.H.
Virology/Molecular Biology Sections

The MDCH virology section has offered hepatitis C virus testing since August 1, 1997. HCV testing was initiated in response to the U.S. Public Health Service Blood Advisory Committee's recommendation that individuals who received a blood transfusion prior to 1992 be tested for exposure to HCV. In July 1998 MDCH announced that this testing was being expanded to include health care facilities who wished to access HCV testing for employees as a part of a bloodborne pathogens control program. This service is provided free to local health departments. Other health care facilities are charged $30 for enzyme immunoassay (EIA) testing and $60 for polymerase chain reaction (PCR) analysis.

Physicians are encouraged to order hepatitis C testing for patients who are at risk based on history or exam. The major risk factors for hepatitis C are:

- Injection of illegal drugs, even once;
- Receipt of clotting factors prior to 1987;
- Long-term hemodialysis;
- Persistent elevation of alanine amino transferase levels; and
- Transfusion or organ transplant prior to July 1992.

Certain others should be tested because of exposure:

- Health care and public safety workers who suffer needle stick, sharps or mucosal exposure to hepatitis C positive blood; and
- Children born to hepatitis C positive women.

Those who test positive for hepatitis C can be counseled about ways to protect their health and the health of those around them. They may also be candidates for specific antiviral therapies (e.g., interferon, riboviran) which have been shown effective in controlling hepatitis C virus.

HCV testing at MDCH is a two step-process. The serum sample is initially screened with two commercially available EIA procedures. Samples that are repeatedly reactive by these assays require confirmatory testing by PCR. The screening EIA procedure detects antibody to HCV while the confirmatory PCR assay detects the presence of viral nucleic acid (RNA).

Because the PCR assay was originally validated using plasma as the sample type, the July 1998 issue of the *LabLink* announced that confirmatory testing of hepatitis C virus testing required the submission of a separate EDTA plasma sample to detect HCV RNA. This article stated that serum samples used to detect antibodies cannot be used in the PCR confirmatory assay. Recognizing that submission of a second specimen is problematic, the molecular biology section has completed a validation study of the use of serum as a specimen for PCR analysis. This study demonstrated that results of PCR analysis were identical for both serum and plasma samples.

MDCH no longer requires the submission of a separate plasma sample for HCV confirmatory testing. Effective immediately HCV positive serum samples will reflex test to the PCR assay. If the sample is repeatedly reactive by EIA, laboratories will receive a report that provides the EIA result along with a statement that confirmation assay results will follow. The PCR test will be completed within one week of the EIA result. A second report providing the results of PCR analysis will be issued upon completion of the confirmatory assay.

Questions concerning HCV antibody testing or specimen submission can be directed to Patty Clark at (517) 335-8102 while questions concerning PCR analysis can be directed to Dr. Jeff Massey at (517) 335-8850.

Patient Residence Information

Effective epidemiology requires accurate information regarding a patient's residence. The county of residence is extremely important so reportable conditions are submitted to the proper county for epidemiological investigation. All CDC and state statistical reports break down disease incidence by county. In past years the submitter's county was used as the default in the absence of patient information. Now with frequent consolidation of multiple laboratories into a central facility, the submitter county is much less accurate.

The laboratory needs to have the patient's city, which our software will link to the correct county, or the patient's county of residence written on all test requests. This will enable MDCH to notify the proper county of any reportable conditions. It will also enhance the accuracy of any state or regional analysis of disease data. Your assistance in this matter is greatly appreciated.

Escherichia coli Shiga-like Toxin Testing

William Schneider
Enteric/STD/Chromatography Unit

The microbiology section has been examining *Escherichia coli* cultures for shiga-like toxins one and two (SLT1 and SLT2) production since January 1, 1997. These toxin-producing organisms are associated with hemorrhagic colitis and hemolytic uremic syndrome (HUS), particularly in children. The latter manifestation may result in kidney malfunction and often death.

All *E. coli* cultures submitted for serotyping are examined by DNA probe for the SLT1 and/or SLT2 genes. Those strains probe positive for SLT1 or SLT2 are serotyped. We have antisera for O157:H7, O111 and O126 strains. Toxin probe positive cultures unable to be serotyped with this antisera are sent to CDC for serotyping. MDCH will report the SLT results of all *E. coli* strains in addition to the serotyping results. Cultures negative for SLT1 and SLT2 are reported "serotype unknown." The following charts contain results of SLT testing from 1997 and 1998 at MDCH laboratories.

1997

Serotype	SLT1 and SLT2 Positive	SLT1 Positive SLT2 Negative	SLT1 Negative SLT2 Positive	Negative for SLT1 and SLT2
O157:H7	95	0	18	0
O157 nonmotile	1	0	4	0
O55:H7	0	0	1	0
O171:H2	0	0	1	0
O26:H11	1	0	0	0
Unknown	0	0	0	376

1998

Serotype	SLT1 and SLT2 Positive	SLT1 Positive SLT2 Negative	SLT1 Negative SLT2 Positive	Negative for SLT1 and SLT2
O157:H7	65	0	8	0
O157 nonmotile	2	0	2	0
O110:H28	0	0	1	0
Unknown	0	0	0	309

In 1997, 121 (24.3%) cultures examined produced shiga-like toxin(s). In 1998, 96 (24.8%) cultures were shiga-like toxin(s) producers. Of these, four were serotypes other than O157. These pathogenic organisms would not have been identified without the initial DNA probe test, followed by restricted *E. coli* serotyping.

Regional Laboratory News

Detuned HIV-1 Testing At Kent County Health Department Laboratory

Kenneth Terpstra, M.S.
Laboratory Manager

In late1998 MDCH successfully competed for funding through CDC to investigate the use of detuned HIV-1 antibody assays. Since the Kent County Regional Laboratory was already performing statewide testing for HIV-1 antibody under a contract with MDCH, it was appropriate the new testing initiative be housed there as well. The laboratory will initially be using the detuned assay to test archived sera from publicly-funded HIV counseling and testing sites that have previously tested positive for HIV-1 antibody. The less sensitive, or detuned, methodology will provide a means to measure seroincidence and identify individuals that have recently seroconverted based on the premise that recent seroconverters will test negative with the less sensitive assay.

Initially this will be a blind study, but test results may later on be released to counseling centers and other testing sites. Identifying new cases could help facilitate partner notification, provide more relevant counseling and allow better focus on control and prevention activities. It is anticipated that CDC will designate the KCHD lab as the Midwest states regional testing site. This will allow the laboratory to draw additional samples from labs in Ohio, Indiana, Illinois, Wisconsin and Minnesota. Currently staff is being trained with the hope of beginning testing in late May or early June.

Pulse Net

Pulse Net is a CDC-sponsored network of public health laboratories that promotes standardized testing and data sharing for rapid foodborne diseases outbreak. This early warning system for multi-state outbreaks targets key bacterial pathogens for DNA fingerprinting using pulsed field gel electrophoresis. This network played an essential role in the recent listeria outbreak investigation nationally and in Michigan. Following public health efforts, including DNA fingerprinting, the case incidence declined due to successful identification and recall of the suspect food, in this case hot dogs and deli meats.

To detect outbreaks it is essential that all isolates of target organism be tested by PFGE and subsequent fingerprints be submitted to the national library. Clinical laboratories are again encouraged to submit all isolates of *Listeria monocytogenes, Shigella sonnei,* and *E. coli* O157:H7 and suspect isolates of *Salmonella* serotype Typhimurium.

Cryptosporidium Isolates Needed

A project to study the epidemiology of Cryptosporidiosis is being conducted through a collaboration of the Michigan Department of Community Health, Michigan State University School of Veterinary Medicine and the University of Michigan School of Public Health. The purpose of this research is to elucidate relationships among human, veterinary and environmental *Cryptosporidium* isolates throughout Michigan. Molecular profiles of these samples will be determined using PCR, RFLP and direct sequencing. These results will be combined with other survey and environmental data to formulate hypotheses regarding transmission mechanisms for the different sources and their role in human disease.

To date very few isolates have been obtained. All positive *Cryptosporidium* stool samples or isolates should be sent to MDCH. This includes past samples that are currently being held and all samples obtained in the future. Samples should be fixed in PVA, not formalin as it may interfere with the method used to type these isolates. Regardless of the fixative, any positive samples will be useful.

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Acting Director, Bureau of Laboratories	**Editor**	**Editorial Review**	**Design and Layout**
Frances Pouch Downes, Dr. P.H.	Susan L. Shiflett	Frances Pouch Downes, Dr. P.H.	Susan L. Shiflett

Michigan Department of Community Health
Bureau of Laboratories
P.O. Box 30035
Lansing, Michigan 48909-7535

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